

Amendments to the Claims:

1. (Currently amended) A method of predicting the likelihood of long-term survival of a breast cancer patient without the recurrence of breast cancer, comprising determining the expression level of ~~one or more~~ prognostic-RNA transcripts or their expression products in a breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their expression products, wherein the prognostic RNA transcript is the transcript of ~~one or more genes selected from the group consisting of: TP53BP2, GRB7, PR, CD68, Bel2, KRT14, IRS1, CTSL, EstR1, Chk1, IGFBP2, BAG1, CEGP1, STK15, GSTM1, FHIT, RIZ1, AIB1, SURV, BBC3, IGF1R, p27, GATA3, ZNF217, EGFR, CD9, and MYBL2, HIF1 α , pS2, ErbB3, TOP2B, MDM2, RAD51C, KRT19, TS, Her2, KLK10, β -Catenin, γ -Catenin, MCM2, PI3KC2A, IGF1, TBP, CCNB1, FBXO5, and DR5,~~

wherein expression of ~~one or more of~~ GRB7, CD68, CTSL, Chk1, AIB1, CCNB1, MCM2, FBXO5, Her2, STK15, SURV, EGFR, and MYBL2, HIF1 α , and TS indicates a decreased likelihood of long-term survival without breast cancer recurrence, ~~and the expression of one or more of TP53BP2, PR, Bel2, KRT14, EstR1, IGFBP2, BAG1, CEGP1, KLK10, β -Catenin, γ -Catenin, DR5, PI3KCA2, RAD51C, GSTM1, FHIT, RIZ1, BBC3, TBP, p27, IRS1, IGF1R, GATA3, ZNF217, CD9, pS2, ErbB3, TOP2B, MDM2, IGF1, and KRT19 indicates an increased likelihood of long-term survival without breast cancer recurrence.~~

2-5. (Canceled)

6. (Original) The method of claim 1 wherein the breast cancer is invasive breast carcinoma.

7. (Canceled)

8. (Original) The method of claim 1 wherein said RNA is isolated from a fixed, wax-embedded breast cancer tissue specimen of said patient.

9. (Original) The method of claim 1 wherein said RNA is isolated from core biopsy tissue or fine needle aspirate cells.

10. (Currently amended) An array comprising polynucleotides hybridizing to two or more of the following genes: ~~α -Catenin, AIB1, AKT1, AKT2, β -actin, BAG1, BBC3, Bcl2, CCNB1, CCND1, CD68, CD9, CDH1, CEGP1, Chk1, CIAP1, cMet.2, Contig 27882, CTSL, DR5, EGFR, EIF4E, EPHX1, ErbB3, EstR1, FBXO5, FHIT1, FRP1, GAPDH, GATA3, G-Catenin, GRB7, GRO1, GSTM1, GUS, HER2, HIF1A, HNF3A, IGF1R, IGFBP2, KLK10, KRT14, KRT17, KRT18, KRT19, KRT5, Maspin, MCM2, MCM3, MDM2, MMP9, MTA1, and MYBL2, P14ARF, p27, P53, PI3KC2A, PR, PRAME, pS2, RAD51C, 3RB1, RIZ1, STK15, STMN3, SURV, TGFA, TOP2B, TP53BP2, TRAIL, TS, upa, VDR, VEGF, and ZNF217.~~

11-13. (Canceled)

15. (Currently amended) The array of claim 10 ~~or claim 14~~ wherein said polynucleotides are cDNAs.

16. (Original) The array of claim 15 wherein said cDNAs are about 500 to 5000 bases long.

17. (Currently amended) The array of claim 10 ~~or claim 14~~ wherein said polynucleotides are oligonucleotides.

18. (Currently amended) The array of claim 17 wherein said oligonucleotides are about 20 to 80 bases long.

19. (Currently amended) The array of claim 10 ~~or claim 14~~ wherein the solid surface is glass.

20. (Original) The array of claim 19 which comprises about 330,000 oligonucleotides.

21. (Currently amended) A method of predicting the likelihood of long-term survival of a patient diagnosed with invasive breast cancer, without the recurrence of breast cancer, comprising the steps of:

- (1) determining the expression levels of the RNA transcripts or the expression products of ~~genes or a gene set selected from the group consisting of CD68, GRB7 and MYBL2~~
- (a) ~~TP53BP2, Bel2, BAD, EPHX1, PDGFR β , DIABLO, XIAP, YB1, CA9, and KRT8;~~
- (b) ~~GRB7, CD68, TOP2A, Bel2, DIABLO, CD3, ID1, PPM1D, MCM6, and WISP1;~~
- (c) ~~PR, TP53BP2, PRAME, DIABLO, CTSL, IGFBP2, TIMP1, CA9, MMP9, and COX2;~~
- (d) ~~CD68, GRB7, TOP2A, Bel2, DIABLO, CD3, ID1, PPM1D, MCM6, and WISP1;~~
- (e) ~~Bel2, TP53BP2, BAD, EPHX1, PDGFR β , DIABLO, XIAP, YB1, CA9, and KRT8;~~
- (f) ~~KRT14, KRT5, PRAME, TP53BP2, GUS1, AIB1, MCM3, CCNE1, MCM6, and ID1;~~
- (g) ~~PRAME, TP53BP2, EstR1, DIABLO, CTSL, PPM1D, GRB7, DAPK1, BBC3, and VEGFB;~~
- (h) ~~CTSL2, GRB7, TOP2A, CCNB1, Bel2, DIABLO, PRAME, EMS1, CA9, and EpCAM;~~
- (i) ~~EstR1, TP53BP2, PRAME, DIABLO, CTSL, PPM1D, GRB7, DAPK1, BBC3, and VEGFB;~~
- (k) ~~Chk1, PRAME, TP53BP2, GRB7, CA9, CTSL, CCNB1, TOP2A, tumor size, and IGFBP2;~~
- (l) ~~IGFBP2, GRB7, PRAME, DIABLO, CTSL, β Catenin, PPM1D, Chk1, WISP1, and LOT1;~~
- (m) ~~HER2, TP53BP2, Bel2, DIABLO, TIMP1, EPHX1, TOP2A, TRAIL, CA9, and AREG;~~
- (n) ~~BAG1, TP53BP2, PRAME, IL6, CCNB1, PAI1, AREG, tumor size, CA9, and Ki67;~~
- (o) ~~CEGP1, TP53BP2, PRAME, DIABLO, Bel2, COX2, CCNE1, STK15, and AKT2, and FGF18;~~
- (p) ~~STK15, TP53BP2, PRAME, IL6, CCNE1, AKT2, DIABLO, eMet, CCNE2, and COX2;~~
- (q) ~~KLK10, EstR1, TP53BP2, PRAME, DIABLO, CTSL, PPM1D, GRB7, DAPK1, and BBC3;~~
- (r) ~~AIB1, TP53BP2, Bel2, DIABLO, TIMP1, CD3, p53, CA9, GRB7, and EPHX1~~
- (s) ~~BBC3, GRB7, CD68, PRAME, TOP2A, CCNB1, EPHX1, CTSL GSTM1, and APC;~~
- (t) ~~CD9, GRB7, CD68, TOP2A, Bel2, CCNB1, CD3, DIABLO, ID1, and PPM1D;~~
- (w) ~~EGFR, KRT14, GRB7, TOP2A, CCNB1, CTSL, Bel2, TP, KLK10, and CA9;~~

- (x) ~~HIF1 α , PR, DIABLO, PRAME, Chk1, AKT2, GRB7, CCNE1, TOP2A, and CCNB1;~~
- (y) ~~MDM2, TP53BP2, DIABLO, Bcl2, AIB1, TIMP1, CD3, p53, CA9, and HER2;~~
- (z) ~~MYBL2, TP53BP2, PRAME, IL6, Bcl2, DIABLO, CCNE1, EPHX1, TIMP1, and CA9;~~
- (aa) ~~p27, TP53BP2, PRAME, DIABLO, Bcl2, COX2, CCNE1, STK15, AKT2, and ID1;~~
- (ab) ~~RAD51, GRB7, CD68, TOP2A, CIAP2, CCNB1, BAG1, IL6, FGFR1, and TP53BP2;~~
- (ac) ~~SURV, GRB7, TOP2A, PRAME, CTSL, GSTM1, CCNB1, VDR, CA9, and CCNE2;~~
- (ad) ~~TOP2B, TP53BP2, DIABLO, Bcl2, TIMP1, AIB1, CA9, p53, KRT8, and BAD;~~
- (ae) ~~ZNF217, GRB7, TP53BP2, PRAME, DIABLO, Bcl2, COX2, CCNE1, APC4, and β -Catenin,~~

in a breast cancer tissue sample obtained from said patient, normalized against the expression levels of all RNA transcripts or their expression products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their products;

- (2) subjecting the data obtained in step (1) to statistical analysis; and
- (3) determining whether the likelihood of said long-term survival has increased or decreased.

22. (Currently amended) A method of predicting the likelihood of long-term survival of a patient diagnosed with estrogen receptor (ER)-positive invasive breast cancer, without the recurrence of breast cancer, comprising the steps of:

- (1) determining the expression levels of the RNA transcripts or the expression products of ~~genes of a gene set selected from the group consisting of~~ CD68; CTSL; FBXO5; SURV; CCNB1; MCM2; Chk1; ~~and~~ MYBL2; HIF1A; eMET; EGFR; TS; STK15; IGF1R; BCL2; HNF3A; TP53BP2; GATA3; BBC3; RAD51C; BAG1; IGF2BP2; PR; CD9; RB1; EPHX1; CEGP1; TRAIL; DR5; p27; p53; MTA; RIZ1; ErbB3; TOP2B; E1F4E, wherein expression of the CD68 and MYBL2 ~~following genes~~ in ER-positive cancer is indicative of a reduced likelihood of survival without cancer recurrence following surgery; ~~CD68; CTSL; FBXO5; SURV; CCNB1; MCM2; Chk1; MYBL2; HIF1A; eMET; EGFR; TS; STK15, and wherein~~ expression of the following genes is indicative of a better prognosis for survival without cancer

recurrence following surgery: ~~IGFR1; BCL2; HNF3A; TP53BP2; GATA3; BBC3; RAD51C; BAG1; IGFBP2; PR; CD9; RB1; EPHX1; CEGP1; TRAIL; DR5; p27; p53; MTA; RIZ1; ErbB3; TOP2B; BIF4E.~~

- (2) subjecting the data obtained in step (1) to statistical analysis; and
- (3) determining whether the likelihood of said long-term survival has increased or decreased.

23. (Original) The method of claim 21 or 22 wherein said statistical analysis is performed by using the Cox Proportional Hazards model.

24. (Currently amended) A method of predicting the likelihood of long-term survival of a patient diagnosed with estrogen receptor (ER)-negative invasive breast cancer, without the recurrence of breast cancer, comprising determining the expression levels of the RNA transcripts or the expression products of ~~genes of the gene set CCND1; UPA; HNF3A; CDH1; Her2; GRB7; AKT1; STMY3; α -Catenin; VDR; GRO1; KT14; KLK10; Maspin; TGF α ; and FRP1,~~ wherein expression of GRB7 ~~the following genes~~ is indicative of a reduced likelihood of survival without cancer recurrence: ~~CCND1; UPA; HNF3A; CDH1; Her2; GRB7; AKT1; STMY3; α -Catenin; VDR; GRO1,~~ and wherein expression of the following genes is indicative of a better prognosis for survival without cancer recurrence: KT14; KLK10; Maspin; TGF α ; and FRP1.

25. (Currently amended) A method of preparing a personalized genomics profile for a patient, comprising the steps of:

- (a) subjecting RNA extracted from a breast tissue obtained from the patient to gene expression analysis;
- (b) determining the expression level of GRB7, CD68 and MYBL2 ~~one or more genes selected from the breast cancer gene set listed in any one of Tables 1-5,~~ wherein the expression level is normalized against a control gene or genes and optionally is compared to the amount found in a breast cancer reference tissue set; and

(c) creating a report summarizing the data obtained by said gene expression analysis.

26. (Original) The method of claim 25, wherein said breast tissue comprises breast cancer cells.

27. (Original) The method of claim 26 wherein said breast tissue is obtained from a fixed, paraffin-embedded biopsy sample.

28. (Original) The method of claim 27 wherein said RNA is fragmented.

29. (Original) The method of claim 25 wherein said report includes prediction of the likelihood of long term survival of the patient.

30. (Original) The method of claim 25 wherein said report includes recommendation for a treatment modality of said patient.

31-33. (Canceled)

34. (Currently amended) A prognostic method comprising:

(a) subjecting a sample comprising breast cancer cells obtained from a patient to quantitative analysis of the expression level of the RNA transcript of ~~at least one gene selected from the group consisting of~~ GRB7, CD68, CTSL, Chk1, AIB1, CCNB1, MCM2, FBXO5, Her2, STK15, SURV, EGFR, and MYBL2, HIF1 α , ~~and~~ TS, or their product, and

(b) identifying the patient as likely to have a decreased likelihood of long-term survival without breast cancer recurrence if the normalized expression levels of said gene or genes, or their products, are elevated above a defined expression threshold.

35. (Canceled)

36. (Original) The method of claim 1 wherein the levels of the RNA transcripts of said genes are normalized relative to the mean level of the RNA transcript or the product of two or more housekeeping genes.

37. (Currently amended) The method of claim 34 ~~or 35~~ wherein the housekeeping genes are selected from the group consisting of glyceraldehyde-3-phosphate dehydrogenase (GAPDH), Cyp1, albumin, actins, tubulins, cyclophilin hypoxanthine phosphoribosyltransferase (HRPT), L32, 28S, and 18S.

38. (Currently amended) The method of claim 34 ~~or 35~~ wherein the sample is subjected to global gene expression analysis of all genes present above the limit of detection.

39. (Original) The method of claim 37 wherein the levels of the RNA transcripts of said genes are normalized relative to the mean signal of the RNA transcripts or the products of all assayed genes or a subset thereof.

40. (Original) The method of claim 38 wherein the level of RNA transcripts is determined by quantitative RT-PCR (qRT-PCR), and the signal is a Ct value.

41-42. (Canceled)

43. (Currently amended) The method of claim 34 ~~or 35~~ wherein said patient is human.

44. (Currently amended) The method of claim ~~[[42]] 43~~ wherein said sample is a fixed, paraffin-embedded tissue (FPET) sample, or fresh or frozen tissue sample.

45. (Currently amended) The method of claim ~~[[42]] 43~~ wherein said sample is a tissue sample from fine needle, core, or other types of biopsy.

46. (Currently amended) The method of claim ~~[[42]] 43~~ wherein said quantitative analysis is performed by qRT-PCR.

47. (Currently amended) The method of claim ~~[[42]] 43~~ wherein said quantitative analysis is performed by quantifying the products of said genes.

48. (Original) The method of claim 45 wherein said products are quantified by immunohistochemistry or by proteomics technology.

49. (Original) The method of claim 34 further comprising the step of preparing a report indicating that the patient has a decreased likelihood of long-term survival without breast cancer recurrence.

50. (Canceled)

51. (Currently amended) A kit comprising one or more of (1) extraction buffer/reagents and protocol; (2) reverse transcription buffer/reagents and protocol; and (3) qPCR buffer/reagents and protocol suitable for performing the method of any one of claims 1, and 34 ~~and 35~~.

52. (New) A method of using GRB7, CD68 and MYBL2 genes or gene products to predict the likelihood of survival of a breast cancer patient without recurrence of breast cancer following surgical removal of the primary tumor comprising predicting a decreased likelihood of long-term survival if the expression level of GRB7, CD68 and MYBL2 or the corresponding expression product is elevated in said subject.

53. (New) A method for predicting the likelihood of survival of a breast cancer patient without recurrence of breast cancer following surgical removal of the primary tumor comprising:
identifying evidence of differential expression of GRB7, CD68 and MYBL2, wherein evidence of increased expression of GRB7, CD68 and MYBL2 indicates that said subject is expected to have a decreased likelihood of long-term survival.

54. (New) The array of claim 10, wherein said immobilized polynucleotides hybridize to polynucleotides from said genes.

55. (New) The array of claim 54, wherein said polynucleotides from said genes comprise modified and unmodified polynucleotides.

56. (New) The method of claim 1, further comprising determining the expression level of one or more prognostic RNA transcripts or their expression products in a breast cancer tissue sample obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said breast cancer tissue sample, or of a reference set of RNA transcripts or their expression products, wherein the prognostic RNA transcript is the transcript of one or more genes selected from the group consisting of: TP53BP2, PR, Bcl2, KRT14, IRS1, CTSL, EstR1, Chk1, IGFBP2, BAG1, CEGP1, STK15, GSTM1, FHIT, RIZ1, AIB1, SURV, BBC3, IGF1R, p27, GATA3, ZNF217, EGFR, CD9, HIF1 α , pS2, ErbB3, TOP2B, MDM2, RAD51C, KRT19, TS, Her2, KLK10, β -Catenin, γ -Catenin, MCM2, PI3KC2A, IGF1, TBP, CCNB1, FBXO5, and DR5.

57. (New) The method of claim 56, wherein expression of one or more of CTSL, Chk1, AIB1, CCNB1, MCM2, FBXO5, Her2, STK15, SURV, EGFR, HIF1 α , and TS indicates a decreased likelihood of long-term survival without breast cancer recurrence, and the expression of one or more of TP53BP2, PR, Bcl2, KRT14, EstR1, IGFBP2, BAG1, CEGP1, KLK10, β -Catenin, γ -Catenin, DR5, PI3KCA2, RAD51C, GSTM1, FHIT, RIZ1, BBC3, TBP, p27, IRS1, IGF1R, GATA3, ZNF217, CD9, pS2, ErbB3, TOP2B, MDM2, IGF1, and KRT19 indicates an increased likelihood of long-term survival without breast cancer recurrence.